Case Report

Sedation with dexmedetomidine target controlled infusion during dental surgery: a retrospective case report

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Background: Dexmedetomidine has emerged as a valuable sedation approach in the context of dental surgery. In the Hannivoort target-controlled infusion (TCI) model is possible to correlate the plasma-site concentration with the sedative effects of dexmedetomidine.

Case Description: In our case report, we employed a dexmedetomidine TCI protocol, involving a loading dose followed by a maintenance infusion. This approach yielded stable hemodynamics, with minimal fluctuations in blood pressure and heart rate. Remarkably, patients within the case report maintained both cooperation and responsiveness while being adequately sedated during their surgical procedures. Prolonged infusions of dexmedetomidine may lead to delayed sedative effects after discontinuation of the drug because of a longer context-sensitive half-life. The use of TCI modes may also be helpful to prevent these adverse effects.

Conclusions: Utilizing dexmedetomidine in conscious sedation for dental surgery offers a range of benefits. These include its analgesic and anxiolytic properties, reduced risk of respiratory depression, and the capacity to promptly awaken patients as necessary. Furthermore, combining dexmedetomidine with midazolam and fentanyl presents a well-balanced sedation strategy that prioritizes patient comfort and safety. The aim of this study is to assess the efficacy of dexmedetomidine when used as a sedative in the TCI model. This evaluation highlights its potential to significantly enhance the dental practice, contributing to improved patient experiences and outcomes during dental procedures.

Keywords: Case report; conscious sedation; dental surgery; dexmedetomidine; target-controlled infusion (TCI)

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Introduction

The number of elderly patients with systemic basal diseases who need invasive dental treatment has increased, as well as the need for dental implants (1). Local anesthesia is typically used during implant procedures, although the length of the procedure and the patient's anxiety may make it very unpleasant. In this way, an intravenous conscious sedation has become an interesting option (2).

The neuroendocrine response, adrenergic discharge, elevated blood pressure, vasovagal responses, reduction of pain tolerance, and the likelihood that nonharmful stimulus may be interpreted as painful are all symptoms of anxiety experienced by patients prior and during to dental treatments (3). For the safe management of intraoperative pain and anxiety during oral surgery operations, conscious intravenous sedation is a viable alternative to general anesthesia (4).

Highlight box

Key findings

- The utilization of dexmedetomidine provides adequate sedation, reduces anxiety levels, and offered effective analgesia during implant procedures. Total intravenous anesthesia (TIVA) is widely used and, when combined with target-controlled infusion (TCI) technology, allows for precise delivery of hypnotic and analgesic medications based on desired plasma or effect-site concentrations, enhancing the accuracy of TIVA.

What is known and what is new?

- Medications employed for conscious sedation in dental practice must prioritize safety, ensuring that patients do not lose consciousness, offering stress reduction without compromising protective reflexes and cognitive function. Since dexmedetomidine causes arousable sedation with minimal respiratory side effects, it is frequently utilized during conscious sedation. Zero-order infusion is the standard infusion technique, however, this conventional infusion process may not foresee clinical outcome and, by extension, adverse effects.
- Target controlled infusion models have the potential to improve the stability and safety of the delivery of anesthetics and sedatives.

What is the implication, and what should change now?

- Hannivoort model provides a safe dexmedetomidine TCI during conscious sedation. The TCI pumps implementation involves an understanding of dexmedetomidine pharmacokinetics and allow the understanding of clinical effects changing drug concentration in plasma. In patients receiving conscious sedation during dental surgery with dexmedetomidine in a TCI model is possible to correlate the plasma-site concentration with the sedative effects and consequently reduce the adverse effects.

A drug-induced condition called intravenous conscious sedation is used during dental surgery to keep patients comfortable, relaxed, and cooperative while reducing fear, worry, and uncertainty (5). A sufficient degree of sedation can reduce the stress response and prevent blood pressure and heart rate increases (3).

Although a variety of agents have been utilized during dental procedures, the best agent and regimen are still unknown. Currently, several anesthetics are utilized to sedate patients during implant procedures (6). Each sedative has distinct qualities, and their combination are used to improve the quality of analgesia and sedation, allowing the reduction of the dose of each one and consequently the adverse effects (7). Typically, the literature suggests a variety of pharmacological procedures to achieve conscious sedation, such as fentanyl and midazolam, midazolam and ketamine, ketamine and propofol, or midazolam alone.

Since dexmedetomidine causes arousable sedation with minimal respiratory side effects, it is frequently utilized during conscious sedation. Zero-order infusion is the standard infusion technique, which is given as a maintenance infusion 10 min following a loading dose. It is challenging to foresee the clinical outcome and, by extension, the negative effects during the conventional infusion process. Since Dyck *et al.* (8) presented the initial PK model in 1993, numerous publications have been made regarding the pharmacokinetics of dexmedetomidine. The dexmedetomidine plasma-site concentration (CP) in patients was most precisely predicted by the Hannivoort *et al.* (9) model; however, no clinical trial validation has been recorded.

Patients receiving conscious sedation during dental surgery were given a target-controlled infusion (TCI) of dexmedetomidine at the CP, and we were able to track the correlation between the sedative effects and the dexmedetomidine CP.

In this case report we aimed to show an effective dose of dexmedetomidine used in the TCI model to induce adequate sedation in patients undergoing invasive dental surgery. We present these cases in accordance with the CARE reporting checklist (available at https://joma.amegroups.com/article/view/10.21037/joma-23-29/rc).

Case presentation

This is a retrospective case report of three patients undergone implant surgery with conscious sedation with dexmedetomidine TCI associated with midazolam and fentanyl small bolus. The first patient was a 74-year-old

Table 1 The main key points

Surgical characteristics	Patient 1	Patient 2	Patient 3
Sex	Female	Male	Male
Age (years)	74	52	54
ASA status	3	1	2
PA (mmHg)	170×100	120×80	126×79
HR (beats/min)	108	50	55
Sedation protocol	Dexmedetomidine (TCI) + midazolam and fentanyl	Dexmedetomidine (TCI) + midazolam and fentanyl	Dexmedetomidine (TCI) + midazolam and fentanyl
Duration of surgery	2 h 10 min	1 h 30 min	2 h 20 min
Time to full recovery	2 h 15 min	50 min	1 h 20 min

ASA, American Society of Anesthesiologist; PA, arterial pressure; HR, heart rate; TCI, target-controlled infusion.

Table 2 Total amounts of DEX, FEN and MDZ and the number of midazolam additional doses

Drugs	Patient 1	Patient 2	Patient 3
Total amount of DEX	110 µg	100 µg	110 µg
Total amount of MDZ	1 mg	2 mg	1 mg
Total amount of FEN	50 µg	100 µg	100 µg
Number of additional MDZ dose	0	1	0

DEX, dexmedetomidine; FEN, fentanyl; MDZ, midazolam.

woman, American Society of Anesthesiologist (ASA) status 3, with hypertension, chronic atrial fibrillation, hypothyroidism and dyslipidemia. In regular use of sertraline, atorvastatin, losartan, atenolol, levothyroxine and apixaban (suspended for 48 h). Echocardiogram showed ejection flexion (FE) =67%, pulmonary artery systolic pressure (PASP) =20 mmHg, moderate aortic insufficiency and dilated left atrium. Her baseline blood pressure was 170×100 mmHg and heart rate were 108 beats/min, respectively. The second patient was a 52-year-old man, ASA status 1. His baseline blood pressure was 120×80 mmHg and heart rate were 50 beats/min, respectively. The third patient was a 54-year-old man, ASA status 2 with history of right nephrectomy due to renal tumor, non-dialytic chronic renal failure (creatinine =1.5), and a moderate obstructive sleep apnea. His baseline blood pressure was 129×79 mmHg and heart rate were 55 beats/min, respectively.

The patients were admitted to the operating room where their vital signs, including noninvasive blood, electrocardiography, heart rate and peripheral oxygen saturation were continuously monitored, and an intravenous line was inserted. An infusion of lactated ringer's solution was started. Oxygen was administered at 2 L/min through a nasal canula. Antibiotic prophylaxis was administered.

The *Table 1* summarize the main key points including ASA, initial blood pressure and heart rate, sedation protocol, duration of surgery and time to full recovery.

Sedation was induced with TCI of dexmedetomidine using a syringe pump. Dexmedetomidine was diluted in 0.9% sodium chloride solution to achieve a concentration of 10 mcg/mL. Dexmedetomidine was started with a target CP of 0.6 ng/mL during approximately 20 min and then, the target CP which is predicted by TCI pump was targeted at 0.3 ng/mL according to the Hannivoort model (9). In our cases, we administered dexmedetomidine at initial loading doses of 1.12 µg/kg/h in the first patient, 1.05 µg/kg/h in the second patient, and, for the third patient, for a 20-min period. Remarkably, patients in our study exhibited minimal variation in heart rate and blood pressure and displayed enhanced cooperation. Bolus of midazolam was administered to maintain sedation and Bolus of fentanyl was available for rescue analgesia intraoperatively. The *Table 2* shows the total amount of dexmedetomidine, midazolam and fentanyl administered during surgery.

Sedation depth was assessed using the observer's assessment of alertness/sedation (OAA/S) scale. 0= does not respond to deep stimulus; 1= does not respond to mild prodding or shaking; 2= respond only after mild prodding or shaking; 3= responds only after name is called loudly or repeatedly; 4= lethargic response to name spoken in normal tone; 5= responds readily to name spoken in normal tone. Approximately 10 min after beginning the infusion, the OAA/S scale reached 3. When adequate sedation was

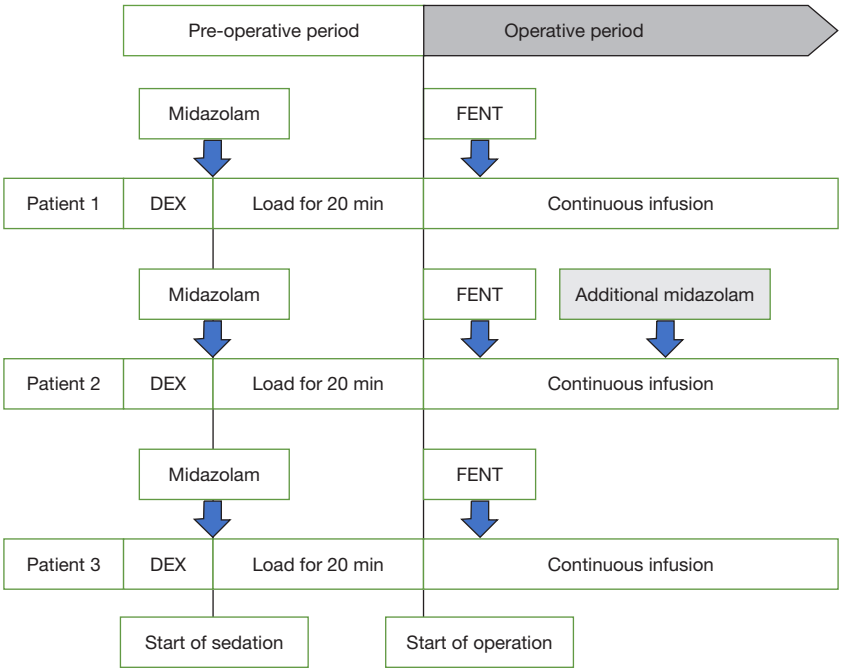

Figure 1 Intravenous sedation protocol in the case report [adapted from Okumura *et al.* (10)]. DEX, dexmedetomidine; FENT, fentanyl.

achieved, local anesthesia was performed.

Blood pressure, heart rate and SpO_2 were stable without electrocardiographic changes throughout the procedure. Oxygen saturation <90% or respiratory depression was treated with supplemental oxygen, verbal stimuli and jaw extension.

The study protocol (*Figure 1*) shows the intravenous sedation performed in the three patients during dental surgery. Dexmedetomidine dose was calculated to target the predicted target CP.

There were no noteworthy changes in systolic blood pressure or heart rate, as illustrated in *Figure 2*.

Intravenous ondansetron was administered to treat postoperative nausea and vomiting.

The management of the postoperative pain involves the administration of dipyrone 2 g, ketorolac 30 mg.

After the operation, the patients were transferred to the post anesthesia care unit, were monitored, and received nasal oxygen supplementation until the Aldrete post anesthesia recovery score reached >9 (full recovery). Clinical recovery from sedation was satisfactory without prolonged sedation.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Sedation techniques play a pivotal role in dental practice training due to their growing significance and utilization (1). Medications and procedures employed for conscious sedation in dental practice must prioritize safety, ensuring that patients do not lose consciousness (11). The appropriate level of sedation should be tailored to each patient, offering stress reduction without compromising protective reflexes and cognitive function (12). Traditional conscious sedation often involves opioid analgesics and benzodiazepines. Recent reviews have highlighted the potential of dexmedetomidine to provide effective analgesia while reducing opioid requirements.

All surgical procedures under conscious sedation were successfully executed, with no significant differences observed in sedation levels using the OAA/S scale among patients. None of the patients experienced severe bradycardia requiring atropine sulfate administration,

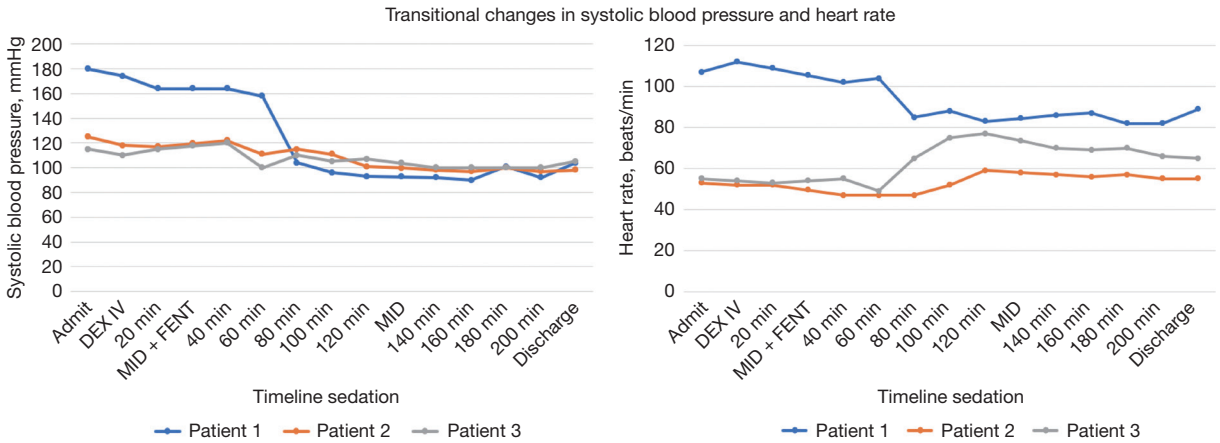

Figure 2 Transitional changes in systolic blood pressure and heart rate, before administration of dexmedetomidine, 10 min after the administration of dexmedetomidine and every 20 min during surgery. DEX, dexmedetomidine; IV, intravenous; MID, midazolam, FENT, fentanyl.

hypotension, or discomfort during the procedure. Patients experience lower levels of anxiety, remained relaxed, calm and collaborative and found the experience agreeable. Patient satisfaction and postoperative hospital stays showed no significant differences. In one instance, a third patient exhibited signs of upper airway obstruction but promptly responded to jaw extension and supplemental oxygen therapy. None of the patients required endotracheal intubation or mechanical ventilation.

Dexmedetomidine, a selective alpha-2 adrenergic receptor agonist, is associated with common adverse effects like bradycardia and hypotension. Elderly patients share physiological traits such as reduced cardiac and respiratory function, slower medication clearance, and prevalent chronic diseases like hypertension. Studies suggest that sedation contributes to maintaining hemodynamic stability and alleviates patient distress (1).

In contrast, the commonly used sedative, propofol, may induce respiratory depression and dose-dependent tongue root settling. Dexmedetomidine, on the other hand, can mitigate stress-induced sympathetic hyperactivity, offering sedation, analgesia, anxiolysis, and mild respiratory depression. It is considered safe for sedating elderly patients and may be associated with lower rates of delirium compared to other sedatives. Dexmedetomidine administration has been shown to reduce the need for fentanyl and pain relief.

Concerns regarding the potential for aspiration and airway obstruction during oral surgery have emerged due to pharyngeal reflex suppression and the risk of respiratory depression as consciousness decreases (10). Dexmedetomidine has gained popularity for conscious sedation due to its unique pharmacological profile. Even at higher doses, patients sedated with dexmedetomidine can be quickly aroused, maintain verbal contact, and do not experience respiratory suppression. These attributes are advantageous in preventing aspiration and airway blockage during dental surgery (10).

Studies suggest that dexmedetomidine, acting as a sedative, reduces pain and inflammatory cytokine levels during implant procedures. Enhanced analgesic effects may be attributed to the regulation of catecholamine release, synergistic analgesic interactions, and a reduction in the stress response to surgery (7). However, it is important to note that dexmedetomidine alone does not induce amnesia, a crucial aspect of these procedures. To address this, small doses of midazolam are administered to prevent patients from remembering the procedure. Midazolam, a benzodiazepine derivative, is used to provide sedation and reduce anxiety without causing cardiorespiratory instability. Combined with sedatives and analgesics, it enhances effectiveness. The addition of low-dose fentanyl does not lead to increased adverse events but offers more effective intra- and postoperative analgesia (10).

To optimize conscious sedation, it is imperative to select an anesthetic agent that reduces patient stress, promotes rapid recovery, and minimizes adverse effects. Intravenous dexmedetomidine, as an adjuvant, reduces opioid and anesthetic requirements in various clinical applications. While opioids are fundamental in pain management, their

Table 3 Intraoperative main adverse effects

Adverse effects	Patient 1	Patient 2	Patient 3
Nausea	0	0	0
Hypotension	0	0	0
Bradicardia	0	0	0
Performed mandibular elevation	0	0	1
Residual intra-operative memory	0	0	0

use can result in various adverse effects such as respiratory depression, nausea, and vomiting. Using a single anesthetic agent may not suffice for all stages of dental surgery performed with conscious sedation. The initial phase of the procedure, involving local anesthesia injections, can be particularly stimulating and painful, necessitating the use of fentanyl to enhance the interaction with dexmedetomidine and to alleviate pain during the intraoperative period.

The recommended loading dose of dexmedetomidine is typically 1.0 mcg/kg over 10 min, with a maintenance infusion dose ranging from 0.2 to 0.7 mcg/kg/h (13). Studies have shown that different dosing strategies can achieve adequate sedation and analgesia while maintaining stable hemodynamics without significant respiratory depression (14). However, it is important to acknowledge that the prolonged half-life of dexmedetomidine raises concerns about recovery times in dental sedation.

As a result of predictable pharmacokinetics and a rapid distribution half-life of 5–6 min after bolus injection, dexmedetomidine may be titrated to a desired effect. Prolonged infusions of dexmedetomidine, however, may lead to delayed sedative effects after discontinuation of the drug because of a longer context-sensitive half-life. The use of TCI modes may also be helpful to prevent these adverse effects and the effects arising from the pharmacological interaction of midazolam, opioid and dexmedetomidine.

Total intravenous anesthesia (TIVA) is widely used and, when combined with TCI technology, allows for precise delivery of hypnotic and analgesic medications based on desired plasma or effect-site concentrations, enhancing the accuracy of TIVA (9). This approach has been employed in developing pharmacokinetic-pharmacodynamic models to predict dexmedetomidine CP accurately, facilitating its administration through TCI (9).

While the most common side effects of dexmedetomidine are bradycardia and hypotension, our observations did not reveal significant variations in systolic blood pressure or heart rate among individuals. Transient hypertension was occasionally observed at the loading dose due to peripheral vasoconstriction, a condition promptly managed by decreasing the infusion rate (13).

Table 3 shows the main intraoperative adverse effects and the frequency in our patients.

It is essential to acknowledge the limitations of this study. The incidence of adverse events may not be reliably detected and may not be generalized to all patients. Further research, with a larger sample size, is needed to fully explore the optimal approach and therapeutic benefits of dexmedetomidine when used in TCI for patients undergoing oral surgery under conscious sedation.

Conclusions

In conclusion, this retrospective case report has demonstrated the effectiveness and safety of conscious sedation using dexmedetomidine with TCI, combined with midazolam and fentanyl, for patients undergoing invasive dental surgery. The utilization of dexmedetomidine provided adequate sedation, reduced anxiety levels, and offered effective analgesia during implant procedures.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://joma.amegroups.com/article/view/10.21037/joma-23-29/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://joma.amegroups.com/article/view/10.21037/joma-23-29/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research

committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Seto M, Kita R, Kondo S. Sedation with dexmedetomidine in elderly patients during dental surgery: a retrospective case series. J Korean Assoc Oral Maxillofac Surg 2019;45:152-7.
2. Pourabbas R, Ghahramani N, Sadighi M, et al. Effect of conscious sedation use on anxiety reduction, and patient and surgeon satisfaction in dental implant surgeries: A systematic review and meta-analysis. Dent Med Probl 2022;59:143-9.
3. Bovaira M, Herrero Babiloni A, Jovaní M, et al. Preoperative Anxiety and Its Influence on Patient and Surgeon Satisfaction in Patients Receiving Dental Implant Surgeries Performed Under Intravenous Conscious Sedation. Int J Oral Maxillofac Implants 2017;32:912-8.
4. González-Lemonnier S, Bovaira-Forner M, Peñarrocha-Diago M, et al. Relationship between preoperative anxiety and postoperative satisfaction in dental implant surgery with intravenous conscious sedation. Med Oral Patol Oral Cir Bucal 2010;15:e379-82.
5. Pourabbas R, Ghahramani N, Sadighi M, et al. Intravenous sedation in dental implant surgeries: A systematic review of hemodynamic effects. J Adv Periodontol Implant Dent 2019;11:49-53.
6. Zhang Y, Li C, Shi J, et al. Comparison of dexmedetomidine with midazolam for dental surgery: A systematic review and meta-analysis. Medicine (Baltimore) 2020;99:e22288.
7. Ito T, Utsumi N, Baba Y, et al. Considerations for Satisfactory Sedation during Dental Implant Surgery. J Pers Med 2023;13:461.
8. Dyck JB, Maze M, Haack C, et al. Computer-controlled infusion of intravenous dexmedetomidine hydrochloride in adult human volunteers. Anesthesiology 1993;78:821-8.
9. Hannivoort LN, Eleveld DJ, Proost JH, et al. Development of an Optimized Pharmacokinetic Model of Dexmedetomidine Using Target-controlled Infusion in Healthy Volunteers. Anesthesiology 2015;123:357-67.
10. Okumura Y, Sato Boku A, Tachi N, et al. Usefulness of Continuous Low-Dose Fentanyl in Combination with Dexmedetomidine and Midazolam for Intravenous Sedation: A Randomised Controlled Trial. Biomed Res Int 2022;2022:2807581.
11. Derkay CS, Bluher AE. Recurrent respiratory papillomatosis: update 2018. Curr Opin Otolaryngol Head Neck Surg 2018;26:421-5.
12. Fiorillo L. Conscious Sedation in Dentistry. Medicina (Kaunas) 2019;55:778.
13. Yu C, Li S, Deng F, et al. Comparison of dexmedetomidine/fentanyl with midazolam/fentanyl combination for sedation and analgesia during tooth extraction. Int J Oral Maxillofac Surg 2014;43:1148-53.
14. Parikh DA, Kolli SN, Karnik HS, et al. A prospective randomized double-blind study comparing dexmedetomidine vs. combination of midazolam-fentanyl for tympanoplasty surgery under monitored anesthesia care. J Anaesthesiol Clin Pharmacol 2013;29:173-8.

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